AMENDMENTS TO THE CLAIMS

1. (withdrawn) A method for detecting malignant hyperplasia in a biological sample, comprising the steps of:

(a) isolating mRNA from said sample; and

(b) detecting hepsin mRNA in said sample, wherein the presence of said hepsin mRNA in said sample is indicative of the presence of malignant hyperplasia, wherein the absense of said hepsin mRNA in said sample is indicative of the absence of malignant hyperplasia.

2. (withdrawn) The method of claim 1, further comprising the step of:

comparing said hepsin mRNA to reference information, wherein said comparison provides a diagnosis of said malignant hyperplasia.

3. (withdrawn) The method of claim 1, further comprising the step of:

comparing said hepsin mRNA to reference information, wherein said comparison determines a treatment of said malignant hyperplasia.

4. (withdrawn) The method of claim 1, wherein said detection of said hepsin mRNA is by PCR amplification.

5. (withdrawn) The method of claim 4, wherein said PCR amplification uses primers selected from the group consisting of SEQ ID No. 8 and SEQ ID No. 9.

6. (withdrawn) The method of claim 1, wherein said biological sample is selected from the group consisting of blood, urine, saliva, tears, interstitial fluid, ascites fluid, tumor tissue biopsy and circulating tumor cells.

7. (withdrawn) A method of inhibiting expression of endogenous hepsin in a cell, comprising the step of:

introducing into said cell a vector comprising a hepsin gene operably linked in opposite orientation to elements necessary for expression, wherein expression of said vector in said cell

produces hepsin antisense mRNA that hybridizes to endogenous hepsin mRNA, thereby inhibiting expression of endogenous hepsin in said cell.

8. (withdrawn) A method of inhibiting hepsin protein in a cell, comprising the step of:

introducing into said cell an antibody which is specific for a hepsin protein or a fragment thereof, wherein binding of said antibody to said hepsin protein or a fragment thereof inhibits hepsin protein in said cell.

9. (withdrawn) The method of claim 8, wherein said hepsin protein fragment is selected from the group consisting of SEQ ID Nos. 28, 29, 30, 31, 88, 89, 108, 109, 128, 129, 148, 149, 150, 151, 152, 153 and 154.

10. (withdrawn) A method of targeted therapy to an individual, comprising the step of:

administering a compound to an individual, wherein said compound has a therapeutic moiety and a targeting moiety specific for hepsin.

11. (withdrawn) The method of claim 10, wherein said targeting moiety is selected from the group consisting of an antibody specific for hepsin and a ligand or ligand binding domain that binds hepsin.

12. (withdrawn) The method of claim 10, wherein said therapeutic moiety is selected from the group consisting of a radioisotope, a toxin, a chemotherapeutic agent, an immune stimulant and a cytotoxic agent.

13. (withdrawn) The method of claim 10, wherein said individual suffers from a cancer selected from the group consisting of ovarian cancer, lung cancer, prostate cancer and colon cancer.

14. (withdrawn) A method of vaccinating an individual against hepsin, comprising the step of:

inoculating an individual with a hepsin protein or fragment thereof that lacks hepsin protease activity, wherein said inoculation with said hepsin protein or fragment thereof elicits an

immune response in said individual, thereby vaccinating said individual against hepsin.

15. (withdrawn) The method of claim 14, wherein said individual has cancer, is suspected of having cancer or is at risk of getting cancer.

16. (withdrawn) The method of claim 14, wherein the length of said hepsin fragment is from 9-residue long to 20-residue long.

17. (withdrawn) The method of claim 16, wherein said 9-residue fragment is selected from the group consisting of SEQ ID Nos. 28, 29, 30, 31, 88, 89, 108, 109, 128, 129, 148, 149, 150, 151, 152, 153 and 154.

18. (currently amended) A method of producing ~~immune-~~activated T cells directed toward hepsin, comprising the steps of:

exposing dendritic cells to a hepsin protein or fragment of SEQ ID NO. 28 or 148 ~~thereof that lacks hepsin protease activity~~, thereby producing activated dendritic cells;

exposing said activated dendritic cells to T cells, wherein said activated dendritic cells would present said hepsin protein or fragment ~~thereof~~ to said T cells, thereby producing ~~immune-~~ activated T cells directed toward said hepsin protein or fragment ~~thereof~~.

19-21. (canceled)

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22. (currently amended) The method of claim 18, wherein said dendritic cells, which are isolated from an individual prior to said exposure to said hepsin or said hepsin fragment, ~~wherein said activated dendritic cells~~ are reintroduced into said individual subsequent to said exposure to said hepsin or said hepsin fragment.

23. (canceled)

24. (withdrawn) An immunogenic composition, comprising a fragment of a hepsin protein and an appropriate adjuvant.

25. (withdrawn) The immunogenic composition of claim 24, wherein the length of said hepsin fragment is from 9-residue long to 20-residue long.

26. (withdrawn) The immunogenic composition of claim 25, wherein said 9-residue fragment is selected from the group consisting of SEQ ID Nos. 28, 29, 30, 31, 88, 89, 108, 109, 128, 129, 148, 149, 150, 151, 152, 153 and 154.

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27. (withdrawn) An oligonucleotide having a sequence complementary to SEQ ID No.188.

28. (withdrawn) A composition comprising the oligonucleotide of claim 27 and a physiologically acceptable carrier.

29. (withdrawn) A method of treating a neoplastic state in an individual in need of such treatment, comprising the step of:

administering to said individual an effective dose of the oligonucleotide of claim 27.

30. (withdrawn) The method of claim 29, wherein said neoplastic state is selected from the group consisting of ovarian cancer, breast cancer, lung cancer, colon cancer and prostate cancer.

31. (withdrawn) A method of screening for compounds that inhibit hepsin activity, comprising the steps of:

(a) contacting a sample comprising hepsin protein with a compound; and

(b) assaying for hepsin protease activity, wherein a decrease in said hepsin protease activity in the presence of said compound relative to hepsin protease activity in the absence of said compound indicates said compound inhibits hepsin activity.

AMENDMENTS TO THE SPECIFICATION

Please amend the figure legend for Figure 1 on page 9 as follows:

Figure 1 shows agarose gel comparison of PCR products derived from normal (lanes 1 and 3) and carcinoma cDNA (lanes 2 and 4). PCR products in lanes 1 and 2 were generated by primer pair SEQ ID NOs. 1 and 2 (sense His and antisense Asp), whereas PCR products in lanes 3 and 4 were generated by primer pair SEQ ID NOs. 1 and 3 (sense His and antisense Ser). AS1, antisense Asp; AS2, antisense Ser.

Please amend the figure legend for Figure 3 on page 9 as follows:

Figure 3 shows agarose gel comparison of PCR products derived from amplification with serine protease redundant primers. [[:]] PCR products were generated from normal cDNA (N, lanes 1 and 3) or tumor cDNA (T, lanes 2 and 4) using primer pair SEQ ID NOs. 1 and 2 (lanes 1 and 2) or primer pair SEQ ID NOs. 1 and 3 (lanes 3 and 4). ~~histidine sense (S1) with aspartic acid antisense (AS1), using normal cDNA (Lane 1) and tumor cDNA (Lane 2); and histidine~~

B3 ~~sense (S1) with serine antisense (AS2), using normal cDNA (Lane 3) and tumor cDNA (Lane 4).~~

Please amend the figure legend for Figure 4 on page 9 as follows:

Figure 4 shows agarose gel comparison of PCR products derived from normal or ovarian tumor cells using ~~amplification with~~ cysteine protease redundant primers. Lane 1, normal ovary; lane 2, ~~low malignant potential tumor; lane 3, serous carcinoma; lane 4,~~ mucinous carcinoma; lane 5, clear cell carcinoma. ~~Normal (Lane 1), low malignant potential (Lane 2), serious carcinoma (Lane 3), mucinous carcinoma (Lane 4), and clear cell carcinoma (Lane 5).~~

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Please amend the figure legend for Figure 5 on page 9 as follows:

Figure 5 shows agarose gel comparison of PCR products derived from normal or ovarian tumor cells using ~~amplification with~~ metallo-protease redundant primers. Lane 1, normal ovary; lane 2, low malignant potential tumor; lane 3, serous carcinoma; lane 4, mucinous carcinoma; lane 5, clear cell carcinoma. ~~Normal (Lane 1), low malignant potential (Lane 2), serious carcinoma (Lane 3), mucinous carcinoma (Lane 4), and clear cell carcinoma (Lane 5).~~

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Please amend the figure legend for Figure 6 on page 10 as follows:

Figure 6 shows ~~amplification with specific primers directed towards the serine protease, hepsin. Expression in~~ agarose gel comparison of PCR products derived from normal ovary (Lanes 1-3), low malignant potential tumors (Lanes 4-8), and ovarian carcinomas (Lanes 9-12) using specific primers directed towards the serine protease hepsin.

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Please amend the figure legend for Figure 7 on page 10 as follows:

Figure 7 shows hepsin expression levels in normal~~, low malignant potential tumors, and ovarian carcinomas. S=serious, M=mucinous, LMP=low malignant potential.~~ ovary or various ovarian carcinoma. LMP, low malignant potential.

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Please amend the figure legend for Figure 8 on page 10 as follows:

Figure 8 shows serine protease stratum corneum chymotrypsin enzyme (SCCE) expression in normal ovary (lanes 1-

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B8 3), low malignant potential tumors (lanes 4-8), and ovarian carcinomas (lanes 9-13).

✓ Please amend the figure legend for Figures 10A-C on pages 10-11 as follows:

Figure 10A shows Northern blot analysis of hepsin expression in normal ovary and ovarian carcinomas. *Lane 1*, normal ovary (case 10); *lane 2*, serous carcinoma (case 35); *lane 3*, mucinous carcinoma (case 48); *lane 4*, endometrioid carcinoma (case 51); and *lane 5*, clear cell carcinoma (case 54). In cases 35, 51 and 54, more than a 10-fold increase in the hepsin 1.8 kb transcript abundance was observed. Figure 10B shows Northern blot analysis of hepsin in normal human fetal tissues. Significant overexpression of the hepsin transcript is noted in both fetal liver and fetal kidney. Figure 10C shows Northern blot analysis of hepsin in adult tissues. ~~Significant overexpression of the hepsin transcript is noted in both fetal liver and fetal kidney.~~ Notably, hepsin overexpression is not observed in normal adult tissue. Slight expression above the background level is observed in the adult prostate.

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Please amend the figure legend for Figures 11A-B on page 11 as follows:

Figure 11A shows a comparison of hepsin cDNA expression in normal ovary (N), mucinous (M) and serous (S) low malignant potential (LMP) tumors and carcinomas (CA) by quantitative PCR. β-tubulin was used as an internal control. Figure 11B shows the ratio of hepsin:β-tubulin expression in normal ovary, LMP tumor, and ovarian carcinoma. Hepsin mRNA expression levels were significantly elevated in LMP tumors, ($p < 0.005$) and carcinomas ($p < 0.0001$) compared to levels in normal ovary. All 10 cases of normal ovaries showed a relatively low level of hepsin mRNA expression.

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Please amend the figure legend for Figures 13A-B on page 12 as follows:

Figure 13A shows a comparison of ~~quantitative PCR of~~ SCCE cDNA expression in normal ovary (N), mucinous (M) and serous (S) low malignant potential (LMP) tumors and carcinomas (CA) by quantitative PCR. ~~from normal ovary and ovarian carcinomas.~~ Figure 13B shows a bar graph comparing the ratio of

B11

B11 SCCE to β-tubulin expression in 10 normal and 44 ovarian carcinoma tissues.

Please amend the figure legend for Figure 14 on page 12 as follows:

B12 Figure 14 shows a comparison ~~by quantitative PCR~~ of protease M expression in normal ovary (N), mucinous (M) and serous (S) low malignant potential (LMP) tumors and carcinomas (CA) by quantitative PCR ~~normal and ovarian carcinoma expression of mRNA for protease M~~.

Please amend the figure legend for Figure 15 on page 12 as follows:

B13 Figure 15 shows the amino acid residues 1-57 of TADG-12 and the site of insertion ~~catalytic domain including an insert~~ near the His 5'-end.

Please amend the figure legend for Figures 17A-B on page 12 as follows:

B14 Figure 17A shows northern blot analysis of ~~the~~ PUMP-1 gene expression in human fetal tissue. Figure 17B shows northern

B14 blot analysis of ~~the~~ PUMP-1 gene expression in normal ovary and ovarian carcinomas.

Please amend the figure legend for Figures 18A-B on pages 12-13 as follows:

Figure 18A shows a comparison of PUMP-1 expression in normal ovary (N), mucinous (M) and serous (S) low malignant potential (LMP) tumors and carcinomas (CA) ~~normal and carcinoma tissues~~ using quantitative PCR with an internal β-tubulin control. Figure 18B shows the ratio of ~~mRNA expression of~~ PUMP-1 mRNA expression compared to that of ~~the~~ internal control β-tubulin in 10 normal and 44 ovarian carcinomas.

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Please amend the figure legend for Figure 19 on page 13 as follows:

Figure 19 shows [[a]] agarose gel comparison of PCR ~~amplified~~ products for the hepsin, SCCE, protease M, PUMP-1 and Cathepsin L genes in normal ovary (N), mucinous (M) and serous (S) low malignant potential (LMP) tumors and carcinomas (CA).

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